AMERICAN VETERINARY MEDICAL ASSOCIATION
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March 15, 2002

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, room 1061
Rockville, MD 20852

Re: Docket No. 88N-0038
Records and Reports Concerning Experience with Approved New Animal Drugs
Interim Final Rule

Dear Sir or Madam:

The American Veterinary Medical Association wishes to comment on the interim final rule addressing the management of adverse event reports following the use of approved new animal drugs. The AVMA is a professional organization of more than 67,000 veterinarians, representing 87% of active veterinarians, dedicated to advancing the science and art of veterinary medicine.

The Association supports the ongoing work of the International Cooperation on Harmonization of Technical Requirements for Approval of Veterinary Medicinal Products (VICH), and encourages it to strive for a set of harmonized pharmacovigilance guidelines for veterinary medicinal products. The AVMA strongly encourages harmonization of terminology and systems to facilitate collection, analysis, and dissemination of product information back to product users. Credible reporting protects the health of animals and the public.

With respect to the FDA interim rule, the AVMA has the following specific comments:

21 CFR §514.3 (h) Definition of *serious adverse drug experience*

The interim rule defines a *serious adverse drug experience* as "an adverse event that is fatal or life-threatening, requires professional intervention, or causes an abortion, stillbirth, infertility, congenital anomaly, prolonged or permanent disability, or disfigurement."

- The phrase "requires professional intervention" should be removed from the definition of *serious adverse drug experience*. There are many professional interventions that are commonly used for events that are, by any definition, not

serious. For example, a veterinarian may administer an antihistamine to a pet that suffers a simple dermal allergic response following drug administration. This professional intervention would make the observation of uncomplicated dermal allergic events a serious adverse drug experience. Therefore, this clause should be removed.

- From a medical perspective, it is not reasonable to include infertility as a serious adverse event. Reports of infertility following drug administration are rarely if ever drug related. There are many types of infertility that would not be considered medically serious. Therefore, to have all reports of infertility to be defined as serious is not medically relevant, nor would it reasonably improve patient safety.

- The definition of *serious adverse drug experience* should include a sentence that addresses the unique aspects of evaluating animals that are housed and managed as a group, as included in the VICH definition. Animals housed and managed as a group must be evaluated differently than a collection of individuals. For example, assume that a 3% death rate is observed in a group of housed and managed animals. Following treatment with a drug the death rate falls to 1%. By the proposed definition, a 1% death rate would be reported as a serious adverse drug experience because fatalities were seen after product use. The more appropriate interpretation would be that use of the product was beneficial, as it reduced the death rate.

- This definition of *serious adverse drug experience* differs from the VICH definition. The AVMA prefers the VICH definition, and recommends that the FDA adopt the VICH definition.

21 CFR §514.80 (b)(2) Fifteen-day NADA/ANADA Alert Report

The proposed 15-day alert report requires reporting of serious adverse events within 15 days regardless of source. This is a completely new regulation that is not harmonized with the currently proposed VICH guidelines. The AVMA encourages the FDA to adhere to the VICH guidelines. The term regardless of source is overly broad. If a drug company employee read about animals that may have experienced adverse events after drug administration on an Internet chat room, would the company be required to report this to the FDA within 15 days? Does this "regardless of source" mean that serious adverse events reported outside the United States of America must be reported to the FDA within 15 days? Such an international requirement is not included in the current VICH draft guidelines on this subject. There is no objective evidence that such a requirement would improve animal safety.

Other comments

The AVMA is examining components of an adverse event reporting system that are required to best serve animal health. The AVMA notes that the following are not

addressed in the interim final rule. We believe that these points should be included in an effective adverse event reporting system. Key points follow:

The Association encourages the FDA to factor adverse events of non-approved animal products into its regulatory strategy for these products. Presently, manufacturers of unapproved products (including animal supplements/nutraceuticals, chemicals, botanicals, herbals, and devices) are under no obligation to report adverse events. The AVMA desires to facilitate adverse experience reporting following the use of non-approved products.

The AVMA seeks a systematic method to report and detect adverse product interactions that may occur when an animal is treated with multiple products that may be regulated by several regulatory agencies. The AVMA encourages the FDA, United States Department of Agriculture, and the Environmental Protection Agency to enhance communication and interaction to facilitate this goal.

The AVMA supports improved analysis of submitted reports and transmittal of medically relevant information back to veterinarians. The AVMA believes that reporting by veterinarians will be enhanced by a convenient pharmacovigilance system that returns clinically relevant information. We strongly support a standard analysis system to determine when reports of an unusual number or severity have been received. A simple listing of recorded events is insufficient to provide proper guidance to practicing veterinarians and insufficient to evaluate whether regulatory action should be considered. A system for analysis of these reports should include, at minimum, a system to categorize the physiologic or anatomic systems involved, a controlled dictionary to record the clinical signs observed and diagnoses made, and a standardized method of analysis intended to determine when reports of an unusual number or severity have been received.

It is imperative that veterinarians receive timely and medically relevant information derived from adverse event reports. The AVMA encourages the FDA to develop methods of rapid and frequent (intervals of 6 months or less) reporting of relevant summaries of adverse events of concern, including those that lead to labeling changes. The sharing of such information is in the interest of animal and public health and serves as an incentive to veterinarians to make additional appropriate adverse event reports.

The AVMA appreciates this opportunity to comment.

Sincerely,

Arthur V. Tennyson, VMD
Assistant Executive Vice President

AVT/ECG

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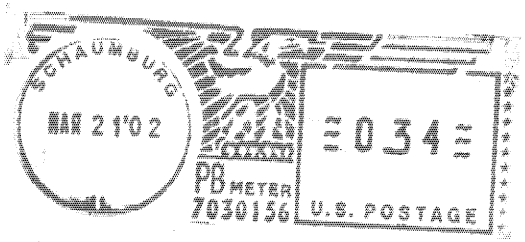

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